

Evaluation of Therapy of Peripheral Polyneuritis

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SUMMARY

*Peripheral polyneuritis is not a disease entity but a mystery. The underlying cause should be searched for, but since often it cannot be found, treatment should be started simultaneously with the search. Conservative measures should be tried first—vitamin B complex, niacin, riboflavin, pyridoxine and thiamine chloride; next, injections of liver extract. Then, if no specific condition amenable to treatment has been discovered and if the patient is seriously incapacitated and becoming worse, hospitalization for trial with BAL is indicated.**

PERIPHERAL polyneuritis is not a disease entity but a syndrome in which the longest neurons in the body are bilaterally, symmetrically affected. It may be due to countless conditions. The effect may be motor, with weakness of the hands and legs, or sensory with glove-and-stocking impairment. Most often it is mixed, both motor and sensory.

The most interesting advance in therapy is the treatment with BAL (2, 3-dimercaptopropanol). This has been found successful not only in cases due to arsenic poisoning, but also in those due to infection or vitamin deficiency.

BAL was developed experimentally as an antidote to arsenic poisoning. The mechanism is as follows: Certain enzymes, including the pyruvate oxidase system, function through their sulfhydryl groups. In arsenic poisoning the arsenic combines with these sulfhydryl groups, making the enzyme inactive. Inactive enzymes disrupt metabolism, and the patient gets sick. BAL has sulfhydryl groups which possess a greater affinity for arsenic than do the sulfhydryl groups contained in enzymes. Therefore, in the presence of BAL, arsenic becomes dissociated from the enzymes to unite with the BAL. The enzymes are liberated. There is renewal of enzyme activity and resumption of metabolic function. The patient improves. The compound formed by the BAL-arsenic combination, BALthioarsenite, is chemically stable, harmless and rapidly excreted by the patient.

BAL is efficacious in the treatment of intoxication with certain heavy metals—arsenic, mercury, gold and antimony. But it is contraindicated for lead neuritis and in cadmium disease. The BAL-lead and BAL-cadmium compounds are more toxic than either lead or cadmium alone.

BAL is useful in heavy metal poisoning because it reactivates the enzyme equilibrium. On the theory that peripheral polyneuritis resulting from causes other than heavy metal intoxication also may be due to disruption of enzyme equilibrium, Nielsen² recommended trial of BAL in cases of peripheral polyneuritis which did not respond to other measures. Treatment with BAL was given at Birmingham Hospital in 1948 by Furmanski,¹ at the Los Angeles County General Hospital, and by Nielsen in private practice. In several instances results were striking. Patients whose condition was getting worse despite administration of large doses of liver extract and vitamins began to improve within a few days of the administration of BAL, and later became ambulatory. In these cases the peripheral polyneuritis was associated with virus infection, and with non-specific anemia and with alcoholism and/or avitaminosis. In all instances symptoms were of recent onset. Therapy is of benefit only when the metabolic disturbance is reversible. With continued disease of the nervous system there is progressive demyelination of the nerves. Eventually no treatment cures.

A syndrome which may be confused with peripheral polyneuritis and which also in the early stages may be amenable to BAL therapy is infectious neuronitis, or the Guillain-Barré syndrome. The patient may have signs of peripheral neuritis; signs of transverse myelitis, with Babinski reaction or inability to void urine; and signs simulating those of anterior poliomyelitis, along with facial or other cranial nerve paralysis. Diagnosis is simplified if suspicion of neuronitis is aroused by acute onset suggestive of virus infection, and by an increase in protein but a low cell count in the spinal fluid. If the patient does not die of the disease—the death rate is about 20 per cent—prognosis for return of function is good. In some cases BAL has proved amazingly effective, in others ineffective.

BAL is available in 10 per cent solution in 20 per cent benzylbenzoate in peanut oil. It should be injected deep into the muscle. Dosage varies with the condition and with the patient. In peripheral polyneuritis 2.5 mg. per kilogram of body weight should be given every six hours. The length of treatment depends on the response of the patient. Occasionally treatment has to be discontinued because of extreme soreness of the gluteal muscles, cold abscesses, vomiting or untoward consequences such as bulbar paralysis. BAL is a potentially hazardous drug. Use of it is indicated in cases of heavy metal poisoning and possibly in fulminating infectious disease of the nervous system. In other cases it should not be used unless conservative measures have proved futile.

Conservative measures include the use of vita-

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min B. This certainly should be tried first, particularly in cases in which there is history of vitamin deficiency or in which associated physical findings are suggestive of it. According to Strauss,³ Wintrobe produced peripheral polyneuritis experimentally with diets adequate in thiamine chloride but deficient in the other vitamin B components. Therefore in the treatment of peripheral polyneuritis all the vitamin B complex should be given—crude vitamin B supplemented by riboflavin, pyridoxine and nicotinic acid as well as thiamine chloride.

Injections of liver extract often have proved helpful even when there was no demonstrable anemia. Patients should receive therapeutic trial with both crude and pure liver extract in massive doses.

The general care of the patient is important: The feet should be splinted to avoid foot drop. During the early irritative stage a cradle should be placed over the limbs to protect them from the irritation of bedclothes, which may cause intolerable pain. Gentle heat may afford relief. Decubitus ulcers should be prevented by judicious padding and frequent changes of position. The patient should be kept clean, dry, comfortable and happy—quite an undertaking if the disease is extensive, with paralysis of the arms as well as of the legs. After the irritative stage is over, light massage and gentle exercise of the affected parts may be instituted and then cautiously increased. Anything that is painful to the patient is contraindicated. Increase of pain is a sign that either the patient or the physiotherapist is doing too much, and that the activity must be reduced or temporarily discontinued. When the patient at last becomes ambulatory he should wear arch supports, since the small muscles of the foot are the last to regain function.

Physical therapy is exceedingly valuable and should be administered by a trained physical therapist. It hastens rehabilitation after an acute episode, and it is the only measure which may help the patient with long-standing peripheral polyneuritis.

Peripheral polyneuritis may be the first manifestation of any of a number of diseases. Therefore, if the cause is not apparent, the temptation to diagnose avitaminosis should be resisted. Instead, careful search for a cause should be made. The possibility of pernicious anemia should be investigated. Blood examination, gastric analysis and therapeutic trial with liver extract should be carried out in cases in

which the cause is obscure. In patients with known pernicious anemia the number of erythrocytes per cu. mm. should be kept over six million if possible in order to prevent central nervous system complications.

Next, diabetes must be considered. Central nervous system disease tends to occur in association with low grade diabetes that is fairly well controlled without insulin. The onset of peripheral polyneuritis may be the first sign of the disease; in a patient known to have diabetes, it may be the signal for more strenuous treatment of that condition.

Hematoporphyrinuria is another condition often associated with peripheral polyneuritis. A 24-hour specimen of urine should be examined for porphyrin bodies. The presence of porphyrin signifies a metabolic disturbance. When this is due to liver dysfunction the patient may be helped by nicotinic acid in doses of at least 50 mg. per day.

Other conditions causing peripheral polyneuritis include hypoglycemia, hyperthyroidism, chronic gastrointestinal or liver disease, acute and chronic febrile illness, diphtheria, leprosy, Boeck's sarcoid disease, parasite infestation, periarteritis nodosa, peripheral vascular disease and malignant neoplasms. These all should be at least considered.

Finally, the possibility of chronic or acute poisoning must be investigated. Considerations in this regard are the medication the patient is taking, arsenic poisoning from the careless use of ant powder or the consumption of unwashed previously sprayed fruit and vegetables, carbon monoxide poisoning, triorthocresyl phosphate contamination of liquor (as a cause of so-called "jake" paralysis) or possibly of cooking oils. (The contamination of cooking oils has been reported in other countries but to date not in the United States.) Also to be considered is absorption of noxious chemicals by inhalation or percutaneous route from insect sprays, dyes, cleaning fluids and similar volatile compounds at home or at work.

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REFERENCES

1. Furmanski, A. R.: BAL therapy of severe peripheral neuropathies, *Arch. Neurol. & Psychiat.*, 60:270, 1948.
2. Nielsen, J. M.: Personal communication.
3. Strauss, Maurice B.: Multiple neuritis. Differentiation of nutritional polyneuritis from other multiple neuritides, *A. Research Nerv. & Mental Dis. Proc.* 1941, 22:141, 1943.

